



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/913,767	01/10/2002	Wolf B. Frommer	056100-5039-US	4393

9629 7590 11/16/2004

MORGAN LEWIS & BOCKIUS LLP
1111 PENNSYLVANIA AVENUE NW
WASHINGTON, DC 20004

EXAMINER

IBRAHIM, MEDINA AHMED

ART UNIT PAPER NUMBER

1638

DATE MAILED: 11/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/913,767	Applicant(s) FROMMER ET AL	
	Examiner Medina A Ibrahim	Art Unit 1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
 - If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
 - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
 - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 01 September 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 23-56 is/are pending in the application.
- 4a) Of the above claim(s) 35,36,40 and 44 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 23-34,37-39,41-43 and 45-56 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 17 August 2001 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

Art Unit: 1638

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group I and SEQ ID NO: 1 in the reply filed on 08/23/04 is acknowledged.

Upon further consideration, it has been determined that the sequences of SEQ ID NO: 2, 6-7 and 10 can be considered with SEQ ID NO: 1 without any search burden, since all sequences are from Arabidopsis encoding proteins of similar function. Claim 40 was inadvertently included in Group I. Claim 40, drawn to the use of nucleic acid encoding a plant or animal nuclear base transporter for the isolation of homologous sequences from bacteria, fungi, plants, animals or human being, will not be examined with claims 23-34, 37-39, 41-43 and 45-56. Under the lack of unity practice, where multiple uses of a product are claimed, Applicant is entitled only for the unity between the product and first method of using the product. Claim 40, drawn to a second method for using the nucleic acid of claim 1, is considered to be a separate invention. The restriction requirement is made FINAL.

Claims 23-56 are pending.

Claims 23-34, 37-39, 41-43 and 45-56 are examined.

Claims 35-36, 40 and 44 are withdrawn from consideration as being drawn to a non-elected invention.

Specification

The specification is objected to for the following informality: the disclosure lacks page and paragraph numbering. Also, at page 7 of the specification, SEQ ID NO: 9 is

Art Unit: 1638

referred as nucleic acid; however, SEQ ID NO: 9 is a protein according to the sequence listings.

Drawings

The drawings are objected to because the detailed description of the drawing should be in English language. Figures 2-5 and 9 of the drawings are described in German language rather than English. Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. The replacement sheet(s) should be labeled "Replacement Sheet" in the page header (as per 37 CFR 1.84(c)) so as not to obstruct any portion of the drawing figures. If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Art Unit: 1638

Claims 23-34, 37-39, 41-43 and 45-56 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 23, 26, 28, 31, 33, and 37-39, 41-43 are indefinite in the recitation of "obtainable" which implies the nucleic acid may or may not be available from its sources. The specification fails to describe under what conditions the desired nucleic acid is "obtainable". Appropriate correction is required to more clearly define the metes and bounds of the claims. Dependent claims 24-25, 27, 29-30, 32, 34, and 45-56 are include in the rejection.

Claims 23, 26, 28, 31, 33, and 37-39, 41-43 are indefinite for failing to recite the specific hybridization/wash conditions required to obtain the desired nucleic acid. There are many different hybridization conditions that vary from one laboratory to another, and the specification fails to define the desired conditions. Therefore, the metes and bounds of the claims are unclear.

Claims 23, 26, 28, 31, 33, and 37-39, 41-43 are indefinite because the metes and bounds " nuclear base transporter" are unclear. According to the definition on page 2 of the specification, " nuclear base transporter" encompasses various proteins involving transport activity of different metabolites essential for cellular functions. However, the claims are so broad in that what is sought for protection remains unclear. The claims also recite "derivative" and it is unclear what the derived product encompasses. Clarification is required to more clearly define the metes and bounds of the claims.

Claims 23, 26, 28, 31, 33, and 37-39, 41-43 are indefinite because a complementary strand cannot code for a protein. For example, if SEQ ID NO: 1 encodes a protein; the complementary or the antisense thereof cannot code for a protein. The claims also recite "plant or animal gene bank". What is encompassed by a "plant or animal gene bank" is not known.

Claim 29 is indefinite because a construct that is in antisense to the regulatory sequence does not make sense.

At claims 30 and 48, a construct that is available in a plasmid is unclear.

Claim 33 is indefinite for failing to recite a proper Markush group. The "host cell" should be deleted to obviate this rejection.

At claims 37, 39, and 43, plants are ---produced--- not "manufactured".

Claims 39, 41-43 provides for the use of nucleic acid or a plant cell, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claims 39, 41-43 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Art Unit: 1638

Claim 51, depending from claim 31 is confusing. It is unclear how a host cell that does not comprise SEQ ID NO: 3, 4 or 5 (claim 31), can again comprise or further comprise the same sequence (claim 51). What is intended by "comprise or further comprise"?

Claims 52-53 are indefinite in the recitation of "a recited nucleic acid ". The metes and bounds of the claim are unclear.

Claims 54-56 are indefinite for failing to recite a proper Markush group. The "host cell" should be deleted to obviate this rejection. Also, the metes and bounds of "comprise or further comprise"? Clarification is required to more clearly define the metes and bounds of the claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 23-34, 37-39, 41-43 and 45-56 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated nucleic acid sequence encoding SEQ ID NO: 8, host cells/plants/parts/seed comprising said nucleic acid sequence, and a method for transforming a plant with said nucleic acid sequence, does not reasonably provide enablement for a nucleic acid sequence encoding a plant or animal nuclear base transporter, fragments and hybridizing sequences and derivatives thereof, host cells/plants/parts, and a method for using said nucleic acids. The specification does not enable any person skilled in the art to which it pertains, or

Art Unit: 1638

with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are broadly drawn to an isolated nucleic acid or fragment thereof that codes for a plant or animal nuclear base transporter comprising a nucleic acid obtainable through complementation of nuclear base transporter deficient host cells with a plant or animal gene bank, a nucleic acid that hybridizes to a nucleic acid encoding SEQ ID NO: 8, and derivatives thereof obtained through substitution, addition, inversion, and/or deletion of one or more bases, and fragments of 20, 50 or 200 bases from said broadly claimed nucleic acids and encoding a plant or animal nuclear transporter, with proviso that the nucleic acid is not SEQ ID NO: 3, 4, or 5. The claims are also drawn to host cells, plants/plant parts and seed comprising said nucleic acids, and process for influencing the nuclear transporter properties of a plant/part/seed by transforming of plants with said nucleic acids.

Applicant teaches isolated nucleic acid sequences from germinal tissues of Arabidopsis encoding SEQ ID NO: 8. The nucleic acid sequences are obtained by functional complementation method using the yeast mutant fcy2 (Example 1). Applicant also teaches analysis of the rate of cytosine uptake in transformed yeast expressing SEQ ID NO: 1 as compared to its wild yeast at various pH levels (Figure 2-3). Figures 2 and 3 show that the cytosine uptake into the transformed yeast was both PH and glucose dependent. Applicant further teaches analysis of the substrate specificity of SEQ ID NO: 1 expressed in the yeast as compared to the yeast's FCY2 transporter (Fig.

Art Unit: 1638

4). Figure 5 shows increased uptake of cytokinin and zeatin in transformed yeast expressing SEQ ID NO: 1.

Applicant has not provided guidance for the obtention and use of the nucleic acids as broadly claimed. Applicant does not teach nucleic acids other than SEQ ID NO: 1 encoding a nuclear base transporter isolated by complementation. Applicant has not provided guidance for complementation systems using host cells other than the yeast mutant *yfc2*. Applicant has not provided guidance for how to identify base transporter deficient host cells that are suitable for the invention as broadly claimed. Applicant has not taught any plant transformed with SEQ ID NO: 1; nor that Applicant teaches a process of influencing nuclear base transport property in a transgenic plant. The specification also discloses SEQ ID NO: 2-7 and 9-10, also from *Arabidopsis*. However, the specification is silent regarding the functional activity of said sequences or their ability to affect nuclear base transport property of a plant is unknown.

The state of the art for isolating nucleic acids with specified function is highly unpredictable. Substantial guidance is required with respect to hybridization/wash conditions that would allow the specific isolation of the target nucleic acid molecules. In the absence of such guidance, one skilled in the art has to proceed with trial and error experimentation to screen through the vast number of cDNA and genomic clones to identify those nucleic acids encoding proteins having the desired functional activity, and to evaluate the ability of said nucleic acids to influence nuclear base transport property in a multitude of transgenic plants.

Art Unit: 1638

The state of the prior art as evidenced by Applicant's own specification (page 1, last paragraph) teaches that very little is known and few transport systems have been described for transport of nuclear bases and their derivatives in plants. Chen et al (Plant physiology 2001, Vol. 125, pp. 1813-1820) teach a putative amino acid transporter from a plant failed to complement the functional activity of a yeast amino acid transporter mutant (Figure 1). See also, Newman et al (Accession no. H76984, deposited January 1998; attached Sequence Search Result, pages 9-10) who teach a nucleic acid sequence with more than 160 contiguous bases of SEQ ID NO: 1 having no known base transport activity.

With respect to the claimed hybridizing sequences, derivatives and fragments, Applicant has not provided guidance for regions in the full-length sequence of SEQ ID NO: 1 that would tolerate modifications. Neither the instant specification nor the prior provides the structural domains involved in the base transport processes. Applicant has not taught which 20, 50 or 200 bases of SEQ ID NO: 1 has the ability to encode a functional polypeptide having the desired activity. Note, the fragments of claims 27 and 45-46 need not be contiguous. Therefore, Applicant has not provided guidance for modifications to SEQ ID NO: 1 that resulted in nucleotide sequences having both the structural and functional limitations as recited in the claims.

While mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions/deletions or multiple modifications as encompassed by the instant claims. One skilled in the art would expect any tolerance to modification for a given DNA/protein to diminish with each further and additional modification or multiple

substitutions/ inversions, additions, deletions. One skilled in the art would have to make all possible nucleotide substitutions/ inversions, additions, deletions in SEQ ID NO: 1 and test all nucleotide sequences that meets the structural limitations to determine which also meet the functional limitation. These tests are considered extensive and undue.

Therefore, given the breadth of the claims, the nature of the invention, the unpredictability with respect to DNA/protein modifications, the limited guidance and working examples in the specification as discussed supra, and the state of the prior art, the claimed invention is not enabled throughout the broad scope. See *In re Wands* 858 F.2d 731, 8USPQ2nd 1400 (Fed. Cir, 1988).

See, also, *Amgen Inc. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ 2d 1016 at 1027 (Fed. Cir. 1991) where the court held that the disclosure of a few gene sequences did not enable claims broadly drawn to any analog thereof.

Written Description

Claims 23-34, 37-39, 41-43, 45-50, 52-53, and 55-56 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to a multitude of isolated nucleic acids and fragments thereof that code for a plant or animal nuclear base transporter obtainable through complementation of nuclear base transporter deficient host cells with any plant

Art Unit: 1638

or animal gene bank; a multitude of nucleic acids that hybridize to a nucleic acid encoding SEQ ID NO: 8 or 9, and derivatives thereof obtained through substitution, addition, inversion, and/or deletion of one or more bases, and fragments of 20, 50 or 200 bases from said broadly claimed nucleic acids and encoding a plant or animal nuclear transporter. The claims are also drawn to a construct or plasmid, host cells, plants/plant parts and seed comprising said nucleic acids, and process for influencing the nuclear transporter properties of a plant/part/seed by transforming a plant with said nucleic acids. In contrast, the specification describes SEQ ID NO: 1 and encoding SEQ ID NO: 8. These are genus claims.

In *Eli Lilly and Co.* 43 USPQ2d 1398 (Fed. Cir. 1997), the court stated:

An adequate written description of a DNA "requires a precise definition, such as by structure, formula, chemical name, or physical properties", not a mere wish or plan for obtaining the claimed chemical invention... Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it; what is required is a description of the DNA itself (43 USPQ2d at 1404).

The court held that held that human insulin-encoding cDNA is not described by prophetic example, which sets forth only a general method for obtaining the human cDNA:

The name cDNA is not itself a written description of that DNA; it conveys no distinguishing information concerning its identity...Describing a method of preparing a cDNA or even describing the protein that the cDNA encodes...does not necessarily describe the DNA itself. No sequence information indicating which nucleotides constitute human cDNA appears in the patent, as appears for rat cDNA....Accordingly, the specification does not provide a written description of human cDNA (43 USPQ2d at 1405).

The description of a single species of rat cDNA was held insufficient to describe the broad genera of vertebrate or mammalian insulin:

"In claims to genetic material...a generic statement such as 'vertebrate insulin cDNA' or 'mammalian insulin cDNA', without more, is not an adequate written

Art Unit: 1638

description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It doesn't define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function...does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is (43 USPQ2d at 1406).

The court continued:

"Thus...a cDNA is not defined by the mere name 'cDNA', even if accompanied by the name of the protein that it encodes, but requires a kind of specificity usually achieved by means of the recitation of the sequence of nucleotides that make up the cDNA...A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus". (43 USPQ2d at 1406). See also where the court teaches that the disclosure of a process for obtaining cDNA from a particular organism and the description of the encoded protein fail to provide an adequate written description of the actual cDNA from the organism which would encode the protein from that organism, despite the disclosure of a cDNA encoding that protein from another organism.

University of California v. Eli Lilly and Co. 43 USPQ2d 1398 (Fed. Cir. 1997) where it states "A description of a genus of cDNA may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus. See also where the court teaches that the disclosure of a process for obtaining cDNA from a particular organism and the description of the encoded protein fail to provide an adequate written description of the actual cDNA from the organism which would encode the protein from that organism, despite the disclosure of a cDNA encoding that protein from another organism.

Applicant has not described the composition and structure of all nucleic acids or fragments thereof that code for a plant or animal nuclear base transporter. Applicant describes the composition and structure of all nucleic acids that hybridize to a nucleic acid encoding SEQ ID NO: 8 or 9, and derivatives thereof. Neither the instant

Art Unit: 1638

specification nor the prior describes the structural domains/features essential for base transport activity of a transporter. In addition, a substantial variation in structures and function is expected among the hybridizing sequences (given the undefined hybridization conditions, see the 112, 2nd rejection above), and sequences that share only 20, 50 or even 200 bases as claimed (note, the fragments of claims 27 and 45-46 need not be contiguous). Therefore, the specification fails to adequately describe the nucleic acid of the invention as broadly claimed. Consequently, the specification has not provided an adequate description for DNA constructs, host cells, and plants comprising said nucleic acids, and a method that employs the same.

Therefore, the claimed invention does not meet the current written description requirements. See, also, the Written description Examination Guidelines published in Federal Registry/Vol. 66, No.4/Friday, January 5, 2001/Notices).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 23-34, 37-39, 41-43, 45-50, 52-53, and 55-56 are rejected under 35 U.S.C. 102(b) as being anticipated by FROMMER et al (US 5, 719, 043).

FROMMER et al teach isolated nucleic acid sequences from Arabidopsis encoding an amino acid transporter obtained by complementation system using amino acid transport deficient yeast cells. The cited reference further teaches a DNA construct

Art Unit: 1638

and plasmid comprising said nucleic acid sequences operable linked to regulatory elements in sense or antisense orientation, to transform prokaryotic and eukaryotic cells. The cited reference further teaches transformation of monocot and dicot plants, and a process of expressing said nucleic acid sequences in a transgenic plant to modify plant nitrogen metabolism (see columns 2, 9-13, 31-32, and Examples 1-5). The prior art nucleic acid sequences anticipate the claimed nucleic acid or fragment thereof that codes for a plant nuclear base transporter obtainable through complementation of nuclear base transporter deficient host cells with a plant or animal gene bank, derivatives, and hybridizing sequences, absent evidence to the contrary. Note, the 112, 2nd rejections above. Note, the fragments of claims 27 and 45-46 need not be contiguous. Therefore, FROMMER et al teach all claim limitations.

Conclusion

Claims 51 and 54 are deemed free of the prior art given the failure of the prior art to teach or reasonably suggest the isolated nucleic acid of SEQ ID NO: 3, 4, or 5.

No claim is allowed.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Medina A. Ibrahim whose telephone number is (571) 272-0797. The Examiner can normally be reached Monday -Thursday from 8:00AM to 5:30PM and every other Friday from 9:00AM to 5:00 PM. Before and after final responses should be directed to fax nos. (703) 872-9306 and (703) 872-9307, respectively.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. Amy Nelson, can be reached at (571) 272-0804.

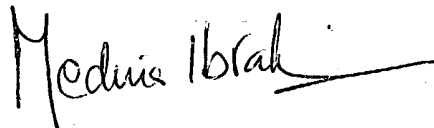
Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status

Art Unit: 1638

information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

11/9/04

Mai

A handwritten signature in black ink, appearing to read "Medina Ibrahim", with a long horizontal flourish extending to the right.

MEDINA A. IBRAHIM
PATENT EXAMINER